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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/874,390	06/04/2001	Henrik Clausen	4305/0J425	5094

7590 01/05/2004

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EXAMINER	
RAO, MANJUNATH N	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 01/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/874,390	CLAUSEN ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 8-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-5,8-18,20,22,23,25,26,28 and 29* is/are allowed.

6)☒ Claim(s) *19,21,24,27 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7-22-03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10-6-03 has been entered.

Claims 1-5 and 8-30 are still at issue and are present for examination.

Applicants' amendments and arguments filed on 10-3-03, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 19 recites the limitation "human" in line 5. There is insufficient antecedent basis for this limitation in the claim.

Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

the invention. Claim 21, line 2, recites the phrase "in a region of the C2/4GnT gene...". It is not clear to the Examiner as to what applicants mean by the above phrase. It is not clear whether applicants mean that said "region" corresponds to exons only in the cDNA or specific exons in the genomic DNA. This confusion arises because SEQ ID NO:1 does not correspond to the genomic sequence (i.e., both introns and exons) of C2/4GnT. Examiner suggests replacing the above phrase with "in a polynucleotide encoding the C2/4GnT polypeptide comprising the steps of,".

Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 21, line 4, recites the phrase "amplifying by PCR a segment of patient's DNA comprising a region that is at least 95% identical to a subsequence of..." It is not clear to the Examiner as to how one can conclude that the patient sample DNA is 95% identical to subsequence of SEQ ID NO:1 even before amplifying the same. Examiner suggests amending the entire phrase as "amplifying by PCR a subsequence of SEQ ID NO:1....".

Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 24, line 2, recites the phrase "in a region of human C2/4GnT gene...". It is not clear to the Examiner as to what applicants mean by the above phrase. It is not clear whether applicants mean that said "region" corresponds to exons only in the cDNA or specific exons in the genomic DNA. This confusion arises because SEQ ID NO:1 does not correspond to

the genomic sequence (i.e., both introns and exons) of C2/4GnT. Examiner suggests replacing the above phrase with "in a polynucleotide encoding the human C2/4GnT polypeptide comprising the steps of,".

Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 24, line 4, recites the phrase "amplifying a segment of ... comprising a region having at least 95% sequence identity with a subsequence of..." It is not clear to the Examiner as to how one can conclude that the patient sample DNA is 95% identical to subsequence of SEQ ID NO:1 even before amplifying the same. Examiner suggests amending the entire phrase as "amplifying a segment of polynucleotide comprising a subseqeunce selected from the group..".

Claim 27 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 19 recites the limitation "human" in line 5. There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 30 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 30 is drawn to a polynucleotide encoding a C2/4GnT transferase wherein said polynucleotide comprises a sequence that is more than 90% identical to nucleotides 1-2319 of SEQ ID NO:1. Applicants have not support for a polynucleotide encoding a C2/4GnT transferase wherein said polynucleotide comprises a sequence that is more than 90% identical to nucleotides 1-2319 of SEQ ID NO:1. Applicants remark that support for the new claim can be found throughout the specification and specifically in originally filed claims 1 and 5 and on page 9 lines 9-10 of the specification. However, a perusal of the original files claims 1 and 5 do not recite the "polynucleotide encoding a C2/4GnT transferase wherein said polynucleotide comprises a sequence that is more than 90% identical to nucleotides 1-2319 of SEQ ID NO:1" language and therefore has no support from the originally filed claims. Similarly, lines 9-10 of page 9 make reference to the EST sequence database match. Such recitation cannot be considered as support for a polynucleotide encoding a C2/4GnT transferase wherein said polynucleotide comprises a sequence that is more than 90% identical to nucleotides 1-2319 of SEQ ID NO:1. Applicants are required to cancel the new matter language.

Claims 21 and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for screening for DNA sequence variations in the cDNA such as the polynucleotide with SEQ ID NO:1, encoding the human C2/C4GnT

polypeptide by amplifying the cDNA by PCR and detecting the variation by DNA sequencing or SSCP does not reasonably provide enablement for such a method to screen variations in a) a genomic DNA encoding the above polypeptide, b)screen sequence variations in an exon and further the specification does not reasonably provide enablement for screening and detecting mismatch mutations. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 21 and 24 are so broad as to encompass methods which have not been taught in the specification. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the different methods broadly encompassed by the claims. Applicants claim a method of screening nucleotide changes n genomic DNA encoding the above polypeptide. However, the specification does not provide the entire genomic sequence of the above gene complete with the sequences of introns and exons. Similarly, claims are drawn to detect nucleotide changes in an exon. However, the specification does not teach the specific exons and their specific sequences for those skilled in the art. The specification provides the information of only a single exon as in figure 8 and provides the sequences of two primers

which can be used. However, the specification is silent regarding the existence of any other exons and their structure. The specification provides the sequence of the cDNA. However, the cDNA information is totally useless for those intending on screening changes in exons or genomic DNA. Similarly, the specification is silent regarding the mismatch mutations. Identification of mismatch mutations without prior knowledge as to which regions of the nucleotide sequence has such mutations is not only unpredictable but also improperly extensive and imposes undue burden on those skilled in the art. Therefore, in order to for the claims to be fully enabled, there is a requirement of knowledge of and guidance with regard to the genomic polynucleotide sequence, the identification of specific exons in the above genomic DNA and identification of mismatch mutations. However, in this case the disclosure is limited to the cDNA sequence only.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for genomic clones or exons with just a cDNA clone. Methods of identifying exons using the cDNA information with a reasonable expectation of success is unpredictable.

The specification therefore does not support the broad scope of the claims which encompass methods of screening genomic DNA, exons and mismatch mutations because the specification does not establish: (A)the specification does not provide a fully annotated genomic sequence information for the above enzyme; (B) the specification does not teach as to how many exons exist in the above gene and the specific sequence of each of the exons; (C) a rational and predictable scheme for identifying mismatch mutations in the above gene; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including methods of screening genomic sequences of the above gene and method of identification of mismatch mutations. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, performing the above methods and obtaining the desired results is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicants have traversed the above rejection arguing that the claim amendments overcomes the above rejection. However, such amendments are not persuasive to overcome the rejection of claim 21 or the new claim 24.

Claim 30 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide comprising nucleotide 1-2319 of SEQ ID NO:1 encoding a polypeptide having C2/4GnT activity and an amino acid sequence SEQ ID NO:2, does not reasonably provide enablement for any polynucleotide comprising a polynucleotide that is more than 90% identical to nucleotides 1-2319 encoding a polypeptide having C2/4GnT activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claim 30 is so broad as to encompass any polynucleotide having 90% identity to to nucleotides 1-2319 encoding a polypeptide having C2/4GnT activity. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. Since the amino acid sequence of an encoded protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of a single enzyme, a C2/4GnT transferase. It would require undue experimentation of the skilled artisan to make and use the claimed polynucleotides. The specification is limited to teaching the use of SEQ ID NO:1 (nucleotides 1-2319) as encoding a polypeptide with a C2/4GnT transferase activity but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of

guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to make and use the full scope of the polynucleotides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any polynucleotide and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any polynucleotide with 90% identity to the nucleotide 1-2319 of SEQ ID NOS:1 because the specification does not establish: (A) regions of the encoded protein structure which may be modified without affecting transferase activity; (B) the general tolerance of such transferases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue on the encoded polypeptide of SEQ ID NO:1 (nucleotides 1-2319) with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims including polynucleotides with an enormous number of modifications to nucleotides 1-2319 of SEQ ID NO:1. The scope of the claim must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

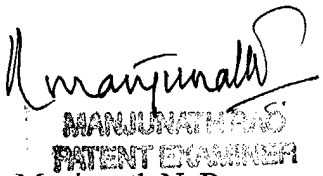
Conclusion

Claims 1-5, 8-18, 20 22, 23, 25-26, and 28-29 are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.



Manjunath N. Rao
December 22, 2003